

FIGURE 1

A: BoNTA(H<sub>e</sub>) synthetic gene (Version #1) SEQ ID NO: 1

GAATTCGAAACGatgCGTCTGCTGTCTACCTTCACTGAATACATCAAGAAC  
ATCATCAATACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGAT  
CGACCTGTCTCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTAACT  
TCGATCCGATCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCC  
AAAATCGAAGTTATCCTGAAGAATGCTATCGTATACAACTCTATGTACG  
AAAACCTTCTCCACCTCCTTCTGGATCCGTATCCCGAAATACTTCAACTCC  
ATCTCTCTGAACAATGAATACACCATCATCAACTGCATGGAAAACAATT  
CTGGTTGGAAAGTATCTCTGAACCTACGGTGAAATCATCTGGACTCTGCAG  
GACACTCAGGAAATCAAACAGCGTGTGTATTCAAATACTCTCAGATGA  
TCAACATCTCTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAAC  
AATCGTCTGAATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACC  
AGAAACCGATCTCCAATCTGGGTAACATCCACGCTTCTAATAACATCATG  
CTTCAATCTGTTTCGACAAAGAAGTGAACGAAAAAGAAATCAAAGACCTG  
TACGACAACCAAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTA  
CCTGCAGTACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAAC  
AAATACGTTGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGA  
AAGGTCCGCGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTTCC  
CTGTACCGTGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACA  
AGGACAATATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTT  
AAGAACAAGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAG  
AAAAGATCTTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCTCAG  
GTAGTTGTAATGAAATCCAAGAACGACGAGGTATCACTAACAATGCA  
AAATGAATCTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTT  
CCACCAGTTCAACAATATCGCTAAACTGGTTGCTTCCAACCTGGTACAATC  
GTCAGATCGAACGTTCTCTCGCACTCTGGGTTGCTCTTGGGAGTTCATC  
CCGTTGATGACGGTTGGGGTGAACGTCCGCTGtaaGAATTC

B: BoNTA(H<sub>e</sub>) encoded protein (Version #1) SEQ ID NO: 2

MRLLSTFTEYIKNIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQI  
QLFNLESSKIEVILKNAIVNSMYENFSTSFWRIPKYFNSISLNNEYTIINCME  
NNSGWKVSLNYGEIHWTLQDTQEIKQRVVFKYSQMINISDYINRWIFVTITNN  
RLNNSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHRYIWIKYFNLF  
DKELNEKEIKDLYDNQSNSGILKDFWGDYLYDKPYMLNLYDPNKEYVDV  
NNVGIRGYMYLKGPRGSVMTTNIYLNSSLYRGTKFIKKYASGNKDNIVRN  
NDRVYINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKN  
DQGITNKCKMNLQDNNNGNDIGFIGFHQFNNAIKLVASNWYNRQIERSRTL  
GCSWEFIPVDDGWGERPL\*

FIGURE 2

**A: BoNTA(H<sub>c</sub>) synthetic gene (version #2) SEQ ID NO: 3**

GAATTCGAAACGatgTCTACCTTCACTGAATACATCAAGAACATCATCAAT  
ACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGATCGACCTGTC  
TCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTTAACTTCGATCCGA  
TCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCCAAAATCGA  
AGTTATCCTGAAGAATGCTATCGTATACAACCTCTATGTACGAAAACCTTCT  
CCACCTCCTTCTGGATCCGTATCCCGAAATACTTCAACTCCATCTCTCTG  
AACAATGAATACACCATCATCAACTGCATGGAAAACAATTCTGGTTGGA  
AAGTATCTCTGAACTACGGTGAAATCATCTGGACTCTGCAGGACACTCA  
GGAAATCAAACAGCGTGTTGTATTCAAATACTCTCAGATGATCAACATCT  
CTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAACAATCGTCTG  
AATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACCAGAAACCGA  
TCTCCAATCTGGGTAACATCCACGCTTCTAATAACATCATGTTCAAACCTG  
GACGGTTGTCGTGACACTACCGCTACATCTGGATCAAATACTTCAATCT  
GTTTCGACAAAGAACTGAACGAAAAAGAAATCAAAGACCTGTACGACAA  
CCAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTACCTGCAGT  
ACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAACAAATACGT  
TGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGAAAGGTCCG  
CGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTTCCCTGTACCG  
TGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACAAGGACAAT  
ATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTTAAGAACAA  
AGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAGAAAAGATC  
TTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCTCAGGTAGTTGT  
AATGAAATCCAAGAACGACCAGGGTATCACTAACAAATGCAAAATGAAT  
CTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTTCCACCAGTT  
CAACAATATCGCTAAACTGGTTGCTTCCAACCTGGTACAATCGTCAGATCG  
AACGTTCTCTCGCACTCTGGGTTGCTCTTGGGAGTTCATCCCGGTTGAT  
GACGGTTGGGGTGAACGTCCGCTGtaaGAATTC

**B: BoNTA(H<sub>c</sub>) encoded protein (Version #2) SEQ ID NO: 4**

MSTFTEYIKNIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQIQLF  
NLESSKIEVILKNAIVYNSMYENFSTSWIRIPKYFNSSISLNNEYTIINCMENNS  
GWKVSILNYGEIHWTLQDTQEIKQRVVFKYSQMINISDYINRWIFVTITNNRLN  
NSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHRYIWIKYFNLFDKE  
LNEKEIKDLYDNQNSGILKDFWGDYLYQYDKPYMLNLYDPNKYVDVNNV  
GIRGYMYLKGRGSVMTTNIYLNSSLYRGTKFIIKKYASGNKDNIVRNNDRV  
YINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKNDQGI  
TNKCKMNLQDNNNGNDIGFIGFHQFNIAKLVASNWYNRQIERSSRTLGCSSW  
EFIPVDDGWGERPL\*

FIGURE 3

**A: BoNTA(H<sub>c</sub>) synthetic gene (Version #3) SEQ ID NO: 5**

GAATTCGAAACGatgGCCTCTACCTTCACTGAATACATCAAGAACATCATC  
AATACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGATCGACCT  
GTCTCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTTAACTTCGATC  
CGATCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCCAAAAT  
CGAAGTTATCCTGAAGAATGCTATCGTATACAACTCTATGTACGAAAAC  
TCTCCACCTCCTTCTGGATCCGTATCCCGAAATACTTCAACTCCATCTCTC  
TGAACAATGAATACACCATCATCAACTGCATGGAAAACAATTCTGGTTG  
GAAAGTATCTCTGAACTACGGTGAAATCATCTGGACTCTGCAGGACACT  
CAGGAAATCAAACAGCGTGTTGTATTCAAATACTCTCAGATGATCAACA  
TCTCTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAACAATCGT  
CTGAATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACCAGAAAC  
CGATCTCCAATCTGGGTAACATCCACGCTTCTAATAACATCATGTTCAAA  
CTGGACGGTTGTCGTGACACTCACCGCTACATCTGGATCAAATACTTCAA  
TCTGTTTCGACAAAGAAGTGAACGAAAAAGAAATCAAAGACCTGTACGAC  
AACCAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTACCTGCA  
GTACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAACAAATAC  
GTTGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGAAAGGTC  
CGCGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTTCCCTGTAC  
CGTGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACAAGGACA  
ATATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTTAAGAAC  
AAAGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAGAAAAGA  
TCTTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCTCAGGTAGTT  
GTAATGAAATCCAAGAACGACCAGGGTATCACTAACAAATGCAAAATGA  
ATCTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTTCCACCAG  
TTCAACAATATCGCTAAACTGGTTGCTTCCAACCTGGTACAATCGTCAGAT  
CGAACGTTTCTCTCGCACTCTGGGTTGCTCTTGGGAGTTCATCCCGGTTG  
ATGACGGTTGGGGTGAACGTCCGCTGtaaGAATTC

**B: BoNTA(H<sub>c</sub>) encoded protein (Version #3) SEQ ID NO: 6**

MASTFTEYIKNIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQIQL  
FNLESSKIEVILKNAIVYNSMYENFSTSWIRIPKYFNSISLNNEYTIINCMENN  
SGWKVSLNYGEIIWTLQDTQEIKQRVVFKEYSQMINISDYINRWIFVTITNNRL  
NNSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHR YIWIKYFNLFDK  
ELNEKEIKDL YDNQSN SGILKDFWGDYLYDKPYYMLNLYDPNKYVDVNN  
VGIRGYMYLKGRGSVMTTNIYLNSSLYRGTKFIIKKYASGNKDNIVRNDR  
VYINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKNDQ  
GITNKCKMNLQDNNGNDIGFIGFHQFNNAKLVASNWYNRQIERSSRTLGC  
SEFIPVDDGWGERPL\*

FIGURE 4

**A: BoNTB(H<sub>c</sub>) synthetic gene SEQ ID NO: 7**

GAATTCACGatGCCAACAAATACAATTCCGAAATCCTGAACAATATCAT  
CCTGAACCTGCGTTACAAAGACAACAATCTGATCGATCTGTCTGGTTACG  
GTGCTAAAGTTGAAGTATACGACGGTGTTGAACTGAATGACAAGAACCA  
GTTCAAACCTGACCTCTTCCGCTAACTCTAAGATCCGTGTTACTCAGAATC  
AGAACATCATCTTCAACTCCGTATTCCTGGACTTCTCTGTTTCCTTCTGGA  
TTCGTATCCCGAAATACAAGAACGACGGTATCCAGAATTACATCCACAA  
TGAATACACCATCATCAACTGCATGAAGAATAACTCTGGTTGGAAGATC  
TCCATCCGCGGTAACCGTATCATCTGGACTCTGATCGATATCAACGGTAA  
GACCAAATCTGTATTCTTCGAATACAACATCCGTGAAGACATCTCTGAAT  
ACATCAATCGCTGGTTCTTCGTTACCATCACCAATAACCTGAACAATGCT  
AAAATCTACATCAACGGTAAACTGGAATCTAATACCGACATCAAAGACA  
TCCGTGAAGTTATCGCTAACGGTGAAATCATCTTCAAACCTGGACGGTGA  
CATCGATCGTACCCAGTTCATCTGGATGAAATACTTCTCCATCTTCAACA  
CCGAACCTGTCTCAGTCCAATATCGAAGAACGGTACAAGATCCAGTCTTA  
CTCCGAATACCTGAAAGACTTCTGGGGTAATCCGCTGATGTACAACAAA  
GAATACTATATGTTCAATGCTGGTAACAAGAACTCTTACATCAAACCTGA  
AGAAAGACTCTCCGGTTGGTGAATCCTGACTCGTTCCAAATACAACCA  
GAACTCTAAATACATCAACTACCGCGACCTGTACATCGGTGAAAAGTTC  
ATCATCCGTCGCAAATCTAACTCTCAGTCCATCAATGATGACATCGTACG  
TAAAGAAGACTACATCTACCTGGACTTCTTCAACCTGAATCAGGAATGG  
CGTGTATACACCTACAAGTACTTCAAGAAAGAAGAAGAAAAGCTTTTCC  
TGGCTCCGATCTCTGATTCCGACGAACTCTACAACACCATCCAGATCAAA  
GAATACGACGAACAGCCGACCTACTCTTGCCAGCTGCTGTTCAAGAAAG  
ATGAAGAATCTACTGACGAAATCGGTCTGATCGGTATCCACCGTTTCTAC  
GAATCTGGTATCGTATTCTGAAGAATACAAGACTACTTCTGCATCTCCAA  
ATGGTACCTGAAGGAAGTTAAACGCAAACCGTACAACCTGAAACTGGGT  
TGCAATTGGCAGTTCATCCCGAAAGACGAAGGTTGGACCGAAtagtaaGAA  
TTC

**B: BoNTB(H<sub>c</sub>) encoded protein SEQ ID NO: 8**

MANKYNSEILNNIILNLRKYDNNLIDLSGYGAKVEVYDGVELNDKNQFKLT  
SSANSKIRVTQNQNIIFNSVFLDFSVSFWIRIPKYKNDGIQNYIHNEYTIINCM  
KNNSGWKISIRGNRIIWTLIDINGKTKSVFFEYNIREDISEYINRFFFVTITNNL  
NNAKIYINGKLESNTDIKDIREVIANGEIIFKLDGDIDRTQFIWMKYFSIFNTEL  
SQSNIEERYKIQSYSEYLKDFWGNPLMYNKEYYMFNAGNKNSYIKLKKDSP  
VGEILTRSKYNQNSKYINYRDL YIGEKFIIRKSNSSQSINDDIVRKEDIYILDF  
FNLNQEWRYVYTYKYFKKEEEKLFLAPISDSDELYNTIQIKEYDEQPTYSCQL  
LFFKDEESTDEIGLIGHRFYESGIVFEEYKDYFCISKWYLKEVKRKPYNLKL  
GCNWQFIPKDEGWTE\*\*

FIGURE 5

**A: BoNTC<sub>1</sub>(H<sub>c</sub>) synthetic gene SEQ ID NO: 9**

GAATTCACGatgACCATCCCATTCAACATCTTCTCCTACACCAACAACCTCC  
CTGTTGAAGGACATCATCAACGAGTACTTCAACAACATCAACGACTCCA  
AGATCCTGTCCCTGCAGAACCGTAAGAACACCTTGGTCGACACCTCCGG  
TTACAACGCCGAGGTCTCCGAGGAGGGTGACGTCCAGCTGAACCCAATC  
TTCCCATTTCGACTTCAAGCTGGGTTCCTCCGGTGAGGACAGAGGTAAGGT  
CATCGTCACCCAGAACGAGAACATCGTCTACAACCTCCATGTACGAGTCC  
TTCTCCATCTCCTTCTGGATCAGAATCAACAAGTGGGTCTCCAACCTTGCC  
AGGTTACACCATCATCGACTCCGTCAAGAACAACCTCCGGTTGGTCCATCG  
GTATCATCTCCAACCTTCTGGTCTTCACCCTGAAGCAGAACGAGGACTCC  
GAGCAGTCCATCAACTTCTCCTACGACATCTCCAACAACGCTCCTGGTTA  
CAACAAGTGGTTCTTCGTCAACCGTCACCAACAACATGATGGGTAACATG  
AAGATCTACATCAACGGTAAGCTGATCGACACCATCAAGGTCAAGGAGT  
TGACCGGTATCAACTTCTCCAAGACCATCACCTTCGAGATCAACAAGATC  
CCAGACACCGGTCTGATCACCTCCGACTCCGACAACATCAACATGTGGA  
TCCGTGACTTCTACATCTTCGCCAAGGAGTTGGACGGTAAGGACATCAA  
CATCCTGTTCAACTCCTTGCAGTACACCAACGTCGTCAAGGACTACTGGG  
GTAACGACCTGAGATACAACAAGGAGTACTACATGGTCAACATCGACTA  
CTTGAACAGATACATGTACGCCAACTCCAGACAGATCGTCTTCAACACC  
AGACGTAACAACAACGACTTCAACGAGGGTTACAAGATCATCATCAAGC  
GTATCAGAGGTAACACCAACGACACCAGAGTCAGAGGTGGTGACATCCT  
GTACTTCGACATGACTATCAACAACAAGGCCTACAACCTGTTTCATGAAG  
AACGAGACCATGTACGCCGACAACCACTCCACCGAGGACATCTACGCCA  
TCGGTCTGCGTGAGCAGACCAAGGACATCAACGACAACATCATCTTCCA  
GATCCAGCCAATGAACAACACTTACTACTACGCTTCCCAGATCTTCAAGT  
CCAACCTTCAACGGTGAGAACATCTCCGGTATCTGTTCCATCGGTACCTAC  
AGATTCCGTCTGGGTGGTGACTGGTACAGACACAACCTACTTGGTTCCAAC  
TGTCAGCAGGGTAACCTACGCCTCCTTGCTGGAGTCCACTTCCACCCACT  
GGGGATTCGTCCCAGTCTCCGAGtaaatagGAATTC

**B: BoNTC<sub>1</sub>(H<sub>c</sub>) encoded protein SEQ ID NO: 10**

MTIPFNIFS YTNNSLLKDIINEYFNNINDSKILSLQNRKNTLVDTSGYNAEVSE  
EGDVQLNPFPDFKLGSSGEDRGKVIVTQENENIVYNSMYESFSISFWIRINK  
WVSNLPGYTIIDSVKNNSGWSIGIISNFLVFTLKQNEDEQSINFSDISNNAP  
GYNKWFFVTVTNNMMGNMKIYINGKLIDTIKVKELTGINFSKTITFEINKIPD  
TGLITSDSDNINMWIRDFYIFAKELDGKDINILFNSLQYTNVVKDYWGNDLR  
YNKEYYMVNIDYLNRYMYANSRQIVFNTRNNNDFNEG YKIIKRIRGNTN  
DTRVRGGDILYFDMTINNKAYNLFMKNETMYADNHSTEDIYAIGLREQTKD  
INDNII FQIQPMNNTYYYASQIFKSNFNGENISGIC SIGTYRFRLGGDWYRHN  
YLVPTVKQGNYASLLESTSTHWGFVPVSE\*\*

FIGURE 6

**A: BoNTD(H<sub>c</sub>) synthetic gene SEQ ID NO: 11**

GAATTCACGatgCGTTTGAAGGCTAAGGTCAACGAGTCCTTCGAGAACAC  
CATGCCATTCAACATCTTCTCCTACACCAACAACCTCCTTGTTGAAGGACA  
TCATCAACGAGTACTTCAACTCCATCAACGACTCCAAGATCTTGTCCTTG  
CAGAACAAGAAGAACGCCTTGGTTCGACACCTCCGGTTACAACGCCGAGG  
TCAGAGTCGGTGACAACGTCCAGTTGAACACCATCTACACCAACGACTT  
CAAGTTGTCCTCTTCCGGTGACAAGATCATCGTCAACTTGAACAACAACA  
TCTTGTACTCCGCCATCTACGAGAACTCCTCTGTCTCCTTCTGGATCAAG  
ATCTCCAAGGACTTGACCAACTCCCACAACGAGTACACCATCATCAACT  
CCATCGAGCAGAACTCCGGTTGGAAGTTGTGTATCCGTAACGGTAACAT  
CGAGTGGATCTTGCAAGGACGTCAACCGTAAGTACAAGTCCTTGATCTTCG  
ACTACTCCGAGTCCTTGTCCCACACCGGTTACACCAACAAGTGGTTCTTC  
GTCACCATCACCAACAACATCATGGGTTACATGAAGTTGTACATCAACG  
GTGAGTTGAAGCAGTCCCAGAAGATCGAGGACCTGGACGAGGTCAAGCT  
GGACAAGACCATCGTCTTCGGTATCGACGAGAACATCGACGAGAACCAG  
ATGTTGTGGATCCGTGACTTCAACATCTTCTCCAAGGAGCTGTCCAACGA  
GGACATCAACATCGTCTACGAGGGTTCAGATCCTGAGGAACGTCATCAAG  
GACTACTGGGGTAACCCACTGAAGTTCGACACCGAGTACTACATCATCA  
ACGACAACATACATCGACCGTTACATCGCCCCAGAGTCCAACGTCCTGGT  
CCTGGTCCAGTACCCTGACCGTTCCAAGCTGTACACCGGTAACCCTATCA  
CCATCAAGTCCGTCTCCGACAAGAACCCCTTACTCCCGTATCCTGAACGGT  
GACAACATCATCCTGCACATGCTGTACAACCTCCCGTAAGTACATGATCAT  
CCGTGACACCGACACCATCTACGCCACCCAGGGTGGTGACTGTTCCAG  
AACTGTGTCTACGCCCTGAAGCTGCAGTCCAACCTGGGTAACCTACGGTAT  
CGGTATCTTCTCCATCAAGAACATCGTCTCCAAGAACAAGTACTGCTCCC  
AGATCTTCTCCTCCTTCCGTGAGAACACCATGCTGCTGGCCGACATCTAC  
AAGCCTTGGCGTTTCTCCTTCAAGAACGCCTACACTCCTGTGCGCGTCAC  
CAACTACGAGACCAAGCTGCTGTCCACCTCCTCCTTCTGGAAGTTCATCT  
CCCGTGACCCAGGTGGGGTCGAGGtaatagGAATTC

**B: BoNTD(H<sub>c</sub>) encoded protein SEQ ID NO: 12**

MRLKAKVNESFENTMPFNIFS YTNNSLLKDIINEYFNSINDSKILSLQNKKNA  
LVDTSGYNAEVRVGDNVQLNTIYTNDFKLSSSGDKIIVNLNNILYSAIYENS  
SVSFWIKISKDLTNSHNEYTIINSIEQNSGWKLCIRNGNIEWILQDVNRKYKS  
LIFDYSESLSHTGYTNKWFFVTITNNIMGYMKLYINGELKQSQKIEDLDEVK  
LDKTIVFGIDENIDENQMLWIRDFNIFSKELSNEDINIVYEGQILRNVIKDYW  
GNPLKFDTEYYIINDNYIDRYIAPESNVLVLVQYPDRSKLYTGNPITIKSVSD  
KNPYSRILNGDNILHMLYNSRKYMIIRDTDTIYATQGGDCSQNCVYALKLQ  
SNLGNYGIGIFSINKIVSKNKYCSQIFSSFRENTMLLADIYKPWRFSFKNAYTP  
VAVTNYETKLLSTSSFWKFI SRDPGWVE\*\*

FIGURE 7

**A: BoNTE(H<sub>2</sub>) synthetic gene SEQ ID NO: 13**

GAATTCACCatgGGAGAGAGTCAGCAAGAACTAAATTCTATGGTAACTGA  
TACCCTAAATAATAGTATTCCTTTTAAGCTTTCTTCTTATACAGATGATAA  
AATTTTAATTTCTACTTCAACAAGTTCTTCAAGAGAATTAAGTCTTCTTC  
CGTTTTAAACATGAGATACAAGAATGATAAATACGTCGACACTTCCGGT  
TACGACTCCAATATCAACATTAACGGTGACGTGTACAAGTACCCAATA  
ACAAAAACCAATTCGGTATCTACAACGACAAGCTTACTGAGCTGAACAT  
CTCTCAAAACGACTACATTATCTACGACAACAAGTACAAGAAGTTCTCTA  
TTTCTTTCTGGGTCAGGATTCCTAACTACGACAACAAGATCGTCAACGTT  
AACAACGAGTACACTATCATCAACTGTATGAGAGACAACAAGTCCGGTT  
GGAAGGTCTCTCTTAACCACAACGAGATCATTTGGACCTTGCAAGACAA  
CGCAGGTATTAACCAAAAAGTTAGCATTCAACTACGGTAACGCAAACGGT  
ATTTCTGACTACATCAACAAGTGGATTTTCGTCCTACTACTAACGACAG  
ATTAGGTGACTCTAAGCTTTACATTAACGGTAAGTTAATCGACCAAAAGT  
CCATTTTAACTTAGGTAACATTCACGTTTCTGACAACATCTTATTCAAG  
ATCGTTAACTGCAGTTACACCAGATACATTGGCATTAGATACTTCAACAT  
TTTCGACAAGGAGTTAGACGAGACCGAGATTCAAACTTTATACAGCAAC  
GAACCTAACACCAATATTTTGAAGGACTTCTGGGGTAACTACTTGCTTTA  
CGACAAGGAATACTACTTATTAACGTTGTTAAAGCCAAACAAGTTTATT  
GATAGGAGAAAGGATTCTACTTTAAGCATTAAACAACATCAGAAGCACTA  
TTCTTTTAGCTAACAGATTATACTCTGGTATCAAGGTAAAGATCCAAAGA  
GTTAACAAGTCTTCTACTAACGATAACCTTGTTAGAAAGAACGATCAGGT  
CTATATTAAGTTCGTCGCTAGCAAGACTCACTTATTCCCATTATATGCTG  
ATACCGCTACCACCAACAAGGAGAAGACCATCAAGATCTCCTCCTCTGG  
CAACAGATTTAACCAAGTCGTCGTTATGAACTCCGTCGGTAACAAGTGT  
CCATGAACTTTAAAAATAATAATGGAAATAATATTGGGTTGTTAGGTTTC  
AAGGCAGATACTGTAGTTGCTAGTACTTGGTATTATACCCACATGAGAG  
ATCACACCAACAGCAATGGATGTTTTTGGAACTTTATTTCTGAAGAACAT  
GGATGGCAAGAAAAAataa  
TagGGATCC GCGGCCGC ACGCGT CCCGGG ACTAGT GAATTC

**B: BoNTE(H<sub>2</sub>) encoded protein SEQ ID NO: 14**

MGESQQELNSMVTDTLNN SIPFKLSSYTDDKILISYFNKFFKRIKSSSVLNMR  
YKNDKYVDTS GYDSNININGDVYKYPTNKNQFGIYNDKLTELNISQNDYIIY  
DNKYKNFSISFWVRIPNYDNKIVNVNNEYTIINCMRDNN SGWKVSLNHNEII  
WTLQDNAGINQKLAFNYGNANGISDYINKWIFVTITNDRLGDSKLYINGNLI  
DQKSILNLGNIHVSDNILFKIVNCSYTRYIGIRYFNIFDKELDETEIQTLYSNEP  
NTNILKDFWGNLYLLYDKEYYLLNVLPNNFIDRRKDSTLSINNIRSTILLANR  
LYSGIKVKIQRVNNSSTNDNLVRKNDQVYINFVASKTHLFLPLYADTATTNKE  
KTIKISSSGNRFNQVVMNSVGNNTMNFKNNGNIGLLGFKADTVVAST  
WYYTHMRDHTNSNGCFWNFISEEHGWQEK\*\*

## AMINO ACID AND DESIGNED NUCLEOTIDE SEQUENCE OF BONTE(Hc)

Asu II  
 TTC GAA AGC ATG ATT TTA ATT TCC TAC TTC AAC AAG TTC TTC AAG AGA ATT AAG TCT TCC GTT TTA AAC ATG AGA TAC AAG AAT GAT AAA TAC GTC  
 M I L I S Y F N K F K R I K S S V L N M R Y K N D K Y V  
 GAC ACT TCC GGT TAC GAC TCC AAT ATC AAC ATT AAC GGT GAC GTG TAC AAG TAC CCA ACT AAC AAA AAC CAA TTC GGT ATC TAC AAC GAC AAG CTT ACT GAG CTG  
 D T S G Y D S N I N I N G D V Y K Y P T N K N Q F G I Y N D K L (T) E L  
 AAC ATC TCT CAA AAC GAC TAC ATT ATC TAC GAC AAC AAG TAC AAG AAC TTC TCT ATT TCT TTC TGG GTC AGA ATT CCT AAC TAC GAC AAC AAG ATC GTC AAC GTT  
 N I S Q N D Y I I Y D N K Y K N F S I S F W V R I P N Y D N K I V N V  
 AAC AAC GAG TAC ACT ATC ATC TGT ATG AGA GAC AAC AAC TCC GGT TGG AAG GTC TCT CTT AAC CAC AAC GAG ATC ATT TGG ACC TTG CAA GAC AAC GCA GGT  
 N I S Q N D Y I I Y D N K Y K N F S I S F W V R I P N Y D N K I V N V  
 ATT AAC CAA AAG TTA GCA TTC AAC TAC GGT AAC GCA AAC GGT ATT TCT GAC TAC ATC AAC AAG TGG ATT TTC GTC ACT ATC ACT AAC GAC AGA TTA GGT GAC TCT  
 I N Q K L A F N Y G N A N G I S D Y I N K W I F V T I T N D R L G D S  
 AAG CTT TAC ATT AAC GGT AAC TTA ATC GAC CAA AAG TCC ATT TTA AAC TTA GGT AAC ATT CAC GTT TCT GAC AAC ATC TTA TTC AAG ATC GTT AAC TCC AGT TAC  
 K L Y I N G N L I D Q K S I L N L G N I H V S D N I L F K I V N C S Y  
 ACC AGA TAC ATT GGC ATT AGA TAC TTC AAC ATT TTC GAC AAG GAG TTA GAC GAG ACC GAG ATT CAA ACT TTA TAC AGC AAC GAA CCT AAC ACC AAT ATT TTG AAG  
 T R Y I G I R Y F N I F D K E L D E I Q T L Y S N E P N T N I L K  
 GAC TTC TGG GGT AAC TAC TTG CTT TAC GAC AAG GAA TAC TAC TTA AAC GTG TTA AAG CCA AAC AAC TTC ATT GAT AGG AGA AAG GAT TCT ACT TTA AGC ATT  
 D F W G N Y L L Y D K E Y Y L L N V L K P N N F I D R R K D S T L S I  
 AAC AAC ATC AGA AGC ACT ATT CTT TTA GGT AAC AGA TTA TAC TCT GGT ATC AAG GTT AAG ATC CAA AGA GTT AAC AAC TCT TCT ACT AAC GAT AAC CTT GTT AGA  
 N N I R S T I L L A N R L Y S G I K V K I Q R V N N S S T N D N L V R  
 AAG AAC GAT CAG GTC TAT ATT AAC TTC GTC GGT AAC AGA ACT CAC TTA TTC CCA TTA TAT GGT GAT ACC GGT ACC AAC AAG GAG AAG ACC ATC AAG ATC TCC  
 K N D Q V Y I N F V A S K T H L F P L Y A D T A T N K E K T I K I S  
 TCC TCT GGC AAC AGA TTT AAC CAA GTC GTC GGT AAC TCC GTC GGT AAC TGT ACC ATG AAC TTT AAA AAT AAT AAT GGA AAT AAT ATT GGG TTG TTA GGT  
 S S G N R F N Q V V M N S V G N N C T M N F K N N N G N N I G L L G  
 TTC AAG GCA GAT ACT GTA GTT GGT AGT ACT TGG TAT TAT ACC CAC ATG AGA GAT CAC ACC AAC AGC AAT GGA TGT TTT TGG AAC TTT ATT TCT GAA GAA CAT GGA  
 F K A D T V V A S T W Y Y T H M R D H T N S N G C F W N F I S E E H G  
 TGG CAA GAA AAA TAA TAG GGA TCC  
 W Q E K ter BamH I

Fig 8



FIGURE 9

**A: BoNTF(H<sub>c</sub>) synthetic gene SEQ ID NO: 15**

GAATTCACGatgTCCTACACCAACGACAAGATCCTGATCTTGTACTTCAAC  
AAGCTGTACAAGAAGATCAAGGACAACCTCCATCTTGGACATGAGATACG  
AAAACAATAAGTTCATCGACATCTCCGGTTACGGTTCCAACATCTCCATC  
AACGGTGACGTCTACATCTACTCCACCAATAGAAACCAGTTCGGAATCT  
ACTCCTCCAAGCCTTCCGAGGTCAACATCGCTCAGAACAAACGACATCAT  
CTACAACGGAAGATAACCAGAACTTCTCCATCTCCTTCTGGGTCCGTATCC  
CAAAGTACTTCAACAAGGTCAACCTGAATAACGAGTACACCATCATCGA  
CTGCATCCGTAACAATAACTCCGGATGGAAGATCTCCCTGAACTACAAC  
AAGATCATCTGGACCCTGCAGGACACCGCCGGTAACAATCAGAAGTTGG  
TCTTCAACTACACCCAGATGATCTCCATCTCCGACTACATCAACAAGTGG  
ATCTTCGTCACCATCACCAATAACCGTTTGGGAAACTCCAGAATCTACAT  
CAACGGTAACTTGATCGACGAGAAGTCCATCTCCAACCTGGGTGACATC  
CACGTCTCCGACAACATTTTGTTCAGATCGTCGGTTGTAACGACACCCG  
TTACGTCGGGATCCGTTACTTCAAAGTCTTCGACACTGAGTTGGGTAAGA  
CCGAGATCGAGACCTTGTACTCCGACGAGCCTGACCCATCCATCCTGAA  
GGACTTCTGGGGTAACTACCTGCTGTACAACAAACGTTACTACTTGCTGA  
ACTTGTTGCGTACCGACAAGTCCATCACCCAGAACTCCAACCTTCTGAAC  
ATCAACCAGCAGAGAGGTGTCTACCAGAAGCCAAACATCTTCTCCAACA  
CCAGATTGTACACCGGAGTCGAGGTCATTATCAGAAAGAACGGATCTAC  
TGATATTTCCAACACCGATAACTTCGTCAGAAAGAACGATCTGGCTTACA  
TCAACGTTGTGACAGAGATGTCGAATACCGTCTGTACGCCGATATCTCT  
ATCGCCAAACCTGAAAAGATCATCAAGCTGATCCGTACCTCTAACTCTA  
ACAACTCTCTGGGACAAATCATCGTCATGGACTCCATCGGTAATAACTGT  
ACCATGAACTTCCAGAACAAACACGGTGGAAACATCGGTTTGTGGGT  
TCCACTCCAACAACTTGGTCGCTTCCTCCTGGTACTACAACAACATCCGT  
AAGAACACCTCCTCCAACGGTTGCTTCTGGTCCTTCATCTCCAAGGAGCA  
CGGTTGGCAGGAGAACTaatagGAATTC

**B: BoNTF(H<sub>c</sub>) encoded protein SEQ ID NO: 16**

MSYTNDKILILYFNKLYKKIKDNSILDMRYENNKFIDISGYGSNISINGDVYIY  
STNRNQFGIYSSKPSEVNIAQNNDIYNGRYQNFSISFWVRIPKYFNKVNLLN  
EYTIIDCIRNNNSGWKISLNYNKIIWTLQDTAGNNQKLVFNQYTMISISDYIN  
KWIFVTITNNRLGNSRIYINGNLIDEKSISNLGDIHVSDNILFKIVGCNDTRYV  
GIRYFKVFDTELKTEIETLYSDEPDPSILKDFWGNLYLLYNKRYLLNLLRT  
DKSITQNSNFLNINQQRGVYQKPNIFSNTRLYTGVEVIIRKNGSTDISNTDNF  
VRKNDLAYINVVDRDVEYRLYADISIAKPEKIIKLRTSNSNNSLGQIIVMDSI  
GNNCTMNFQNNNGGNIGLLGFHSNNLVASSWYYNNIRKNTSSNGCFWSFIS  
KEHGWQEN\*\*

FIGURE 10

**A: BoNTG(H<sub>c</sub>) synthetic gene SEQ ID NO: 17**

GAATTCACGatgAAGGACACCATCCTGATCCAGGTCTTCAACAACACTACATC  
TCCAACATCTCCTCCAACGCCATCCTGTCCCTGTCCTACCGTGGTGGTCG  
TCTGATCGACTCCTCCGGTTACGGAGCCACCATGAACGTCGGTTCGGACG  
TCATCTTCAACGACATCGGTAACGGTCAGTTCAAGCTGAACAACCTCCGA  
GAACTCCAACATCACCGCCCACCAGTCCAAGTTCGTCGTCTACGACTCCA  
TGTTTCGACAACCTTCTCCATCAACTTCTGGGTCCGTACCCCAAAGTACAAC  
AACAAACGACATCCAGACCTACCTGCAGAACGAGTACACCATCATCTCCT  
GTATCAAGAACGACTCCGGTTGGAAGGTCTCCATCAAGGGAAACCGTAT  
CATCTGGACCCTGATCGACGTCAACGCCAAGTCCAAGTCCATCTTCTTCG  
AGTACTCCATCAAGGACAACATCTCCGACTACATCAACAAGTGGTTCTCC  
ATCACCATCACCAACGACCGTCTGGGTAACGCCAACATCTACATCAACG  
GTTCCCTGAAGAAGTCCGAGAAGATCCTGAACCTGGACCGTATCAACTC  
CTCCAACGACATCGACTTCAAGCTGATCAACTGTACCGACACCACCAAG  
TTCGTCTGGATCAAGGACTTCAACATCTTCGGTCGTGAGCTGAACGCCAC  
CGAGGTCTCCTCCCTGTACTGGATCCAGTCCTCCACCAACACCCTGAAGG  
ACTTCTGGGGAAACCCACTGCGTTACGACACCCAGTACTACCTGTTCAAC  
CAGGGTATGCAGAACATCTACATCAAGTACTTCTCCAAGGCCTCCATGG  
GTGAGACCGCCCCTCGTACCAACTTCAACAACGCCGCCATCAACTACCA  
GAACCTGTACCTGGGTCTGCGTTTCATCATCAAGAAGGCCTCCAACCTCCC  
GTAACATCAACAACGACAACATCGTCCGTGAGGGTGACTACATCTACCT  
GAACATCGACAACATCTCCGACGAGTCCTACCGTGTCTACGTCCTGGTCA  
ACTCCAAGGAGATCCAGACCCAGCTGTTCCCTGGCCCCAATCAACGACGA  
CCCTACCTTCTACGACGTCTGCGAGATCAAGAAGTACTACGAGAAGACC  
ACCTACAACCTGTCAGATCCTGTGCGAGAAGGACACCAAGACCTTCGGAC  
TGTTTCGGTATCGGTAAGTTCGTCAAGGACTACGGTTACGTCTGGGACACC  
TACGACAACCTACTTCTGTATCTCCCAGTGGTACCTGCGTCGTATCTCCGA  
GAACATCAACAAGCTGCGTCTGGGATGTAACCTGGCAGTTCATCCCAGTC  
GACGAGGGTTGGACCGAGtaaatagGAATTC

**B: BoNTG(H<sub>c</sub>) encoded protein SEQ ID NO: 18**

MKDTILIQVFNNYISNISSNAILSLSYRGGRLIDSSGYGATMNVGSDVIFNDIG  
NGQFKLNSENSENITAHQSKFVVYDSMFDNFSINFWVRTPKYNNNDIQTYL  
QNEYTHISCIKND SGWKVSIKGNRIIWTIDVNAKSKSIFFEYSIKDNISDYINK  
WFSITITNDRLGNANIYINGSLKKSEKILNLDRLINSSNDIDFKLINCTDITKFKV  
WIKDFNIFGRELNATEVSSLYWIQSSTNTLKD F WGNPLRYDTQYYLFNQGM  
QNIYIKYFSKASMGETAPRTNFNNAAINYQNL YLGLRFIKKASNSRNINNDN  
IVREGDYIYLNIDNISDES YRVYVLVNSKEIQTQLFLAPINDDPTFYDVLQIKK  
YYEKTTYNCQILCEKDTKTFGLFGIGKFVKDYGYVWDTYDNYFCISQWYLR  
RISENINKLRLGNCNWQFIPVDEGWTE\*\*

FIGURE 11

**A: BoNTA(H<sub>N</sub>) synthetic gene SEQ ID NO: 19**

atgGCTCTGAACGACCTGTGCATCAAAGTTAACAACCTGGGACCTGTTCTTC  
TCCCCGTCTGAAGACAACCTTCACTAACGACCTGAACAAAGGCGAAGAAA  
TCACCTCCGACACTAACATCGAAGCTGCTGAAGAAAACATCTCTCTGGA  
CCTGATCCAGCAGTACTACCTGACTTTCAACTTCGACAACGAACCGGAA  
AACATCTCCATCGAAAACCTGTCTTCCGACATCATCGGTCAGCTGGAAC  
GATGCCGAACATCGAACGCTTCCCGAACGGCAAGAAATACGAACACGGTA  
AAATACACCATGTTCCACTACCTGCGTGCTCAGGAATTTCGAACACGGTA  
AATCTCGTATCGCTCTGACTAACTCCGTTAACGAAGCTCTGCTGAACCCG  
TCTCGCGTTTACACCTTCTTCTCTTCCGACTACGTTAAGAAAGTTAACAA  
AGCTACTGAAGCTGCTATGTTCTGGGTTGGGTTGAACAGCTGGTTTACG  
ACTTCACCGACGAAACTTCTGAAGTTTCCACCACTGACAAAATCGCTGAC  
ATCACTATCATCATCCCGTACATCGGCCCGGCTCTGAACATCGGTAACAT  
GCTGTACAAAGACGACTTCGTTGGTGCTCTGATCTTCTCTGGCGCTGTTA  
TCCTGCTGGAATTCATCCCGGAAATCGCTATCCCGGTTCTGGGTACCTTC  
GCTCTGGTTTCTACATCGCTAACAAAGTTCTGACTGTTTCAGACCATCGA  
CAACGCTCTGTCTAAACGTAACGAAAAATGGGACGAAGTTTACAAATAC  
ATCGTTACTAACTGGCTGGCTAAAGTTAACACTCAGATCGACCTGATCCG  
TAAGAAGATGAAAGAAGCTCTGGAAAACCAGGCTGAAGCTACTAAAGC  
TATCATCAACTACCAGTACAACCAGTACACCGAAGAAGAAAAGAACAAC  
ATCAACTTCAACATCGATGACCTGTCTCTAACTGAACGAATCCATCAA  
CAAAGCTATGATCAACATCAACAAATTCCTGAACCAGTGCTCTGTTTCT  
ACCTGATGAACTCTATGATCCCGTACGGCGTTAAACGCCTGGAAGACTTC  
GACGCTTCCCTGAAAGACGCTCTGCTGAAATACATCCGTGACAACTACG  
GTACTCTGATCGGCCAGGTTGACCGTCTGAAAGACAAGGTTAACAACAC  
CCTGTCTACTGACATCCCGTTCCAGCTGTCCAAATACGTTGACAACCAAGta  
a

**B: BoNTA(H<sub>N</sub>) encoded protein SEQ ID NO: 20**

MALNDLCIKVNNWDLFFSPSEDNFTNDLNKGEEITSDTNIEAAEENISLDLIQ  
QYYLTFNFDNEPENISIENLSSDIIGQLELMPNIERFPNGKKYELDKYTMFHY  
LRAQEFEGHKSRIALTNSVNEALLNPSRVYTFSSDYVKKVNKATEAAMFL  
GWVEQLVYDFTDETSEVSTTDKIADITIIPYIGPALNIGNMLYKDDFVGALIF  
SGAVILLEFIPEIAPVLGTFALVSYIANKVLTQVQIDNALSQRNEKWDEVYK  
YIVTNWLAKVNTQIDLIRKKMKEALENQAEATKAIINYQYNQYTEEEKNNI  
NFNIDDLSSKLNESINKAMININKFLNQCSVSYLMNSMIPYGVKRLEDFFDASL  
KDALLKYIRDNYGTLIGQVDRCLKDKVNNTLSTDIPFQLSKYVDNQ\*

FIGURE 12

**A: BoNTB(H<sub>N</sub>) synthetic gene SEQ ID NO: 21**

atgGCTCCAGGAATCTGTATCGACGTCGACAACGAGGACTTGTTCTTCATC  
GCTGACAAGAACTCCTTCTCCGACGACTTGTCCAAGAACGAGAGAATCG  
AGTACAACACCCAGTCCAACCTACATCGAGAACGACTTCCCAATCAACGA  
GTTGATCTTGGACACCGACTTGATCTCCAAGATCGAGTTGCCATCCGAGA  
ACACCGAGTCCTTGACTGACTTCAACGTCGACGTCCCAGTCTACGAGAA  
GCAACCAGCTATCAAGAAGATTTTCACCGACGAGAACACCATCTTCCAA  
TACCTGTACTCTCAGACCTTCCCTTTGGACATCAGAGACATCTCCTTGAC  
CTCTTCCTTCGACGACGCCCTGCTGTTCTCCAACAAGGTCTACTCCTTCTT  
CTCCATGGACTACATCAAGACTGCTAACAAGGTCGTCGAGGCCGGTTTG  
TTCGCTGGTTGGGTCAAGCAGATCGTCAACGATTTTCGTCATCGAGGCTAA  
CAAGTCCAACACCATGGACAAGATTGCCGACATCTCCTTGATTGTCCCAT  
ACATCGGTTTGGCCTTGAACGTCGGTAACGAGACCGCCAAGGGTAACTT  
CGAGAACGCTTTTCGAGATCGCTGGTGCCTCCATCTTGTTGGAGTTCATCC  
CAGAGTTGTTGATCCAGTCGTCGGTGCCTTCTTGTTGGAGTCCTACATC  
GACAACAAGAACAAGATCATCAAGACCATCGACAACGCTTTGACCAAGA  
GAAACGAGAAGTGGTCCGACATGTACGGTTTGATCGTCGCCCAATGGTT  
GTCCACCGTCAACACCCAATTCTACACCATCAAGGAGGGTATGTACAAG  
GCCTTGAACCTACCAGGCCCAAGCTTTGGAGGAGATCATCAAGTACAGAT  
ACAACATCTACTCCGAGAAGGAGAAGTCCAACATTAACATCGACTTCAA  
CGACATCAACTCCAAGCTGAACGAGGGTATTAACCAGGCCATCGACAAC  
ATCAACAACCTTCATCAACGGTTGTTCCGTCTCCTACTTGATGAAGAAGAT  
GATTCCATTGGCCGTCGAGAAGTTGTTGGACTTCGACAACACCCTGAAG  
AAGAACTTGTTGAACTACATCGACGAGAACAAAGTTGTACTTGATCGGTT  
CCGCTGAGTACGAGAAGTCCAAGGTCAACAAGTACTTGAAGACCATCAT  
GCCATTCGACTTGTCCATCTACACCAACGACACCATCTTGATCGAGATGT  
TCtaa

**B: BoNTB(H<sub>N</sub>) encoded protein SEQ ID NO: 22**

MAPGICIDVDNEDLFFIADKNSFSDDL SKNERIEYNTQS NYIENDFPINELILD  
TDLISKIELPSENTESLTD FNVDVPVYEKQPAIKKIFTDENTIFQYLYSQTFLD  
IRDISLTSSFDDALLFSNKVYSFFSMDYIKTANKVVEAGLFAGWVKQIVNDF  
VIEANKSNTMDKIADISLIVPYIGLALNVGNETA KGNFENAFEIAGASILLEFI  
PELLIPVVGAFLLSYIDNKNKIIKTIDNALTKRNEKWSDMYGLIVAQWLST  
VNTQFYTIKEGMYKALNYQAQALEEIIKYRYNIYSEKEKSNINIDFNDINSKL  
NEGINQAIDNINNFIN GCSVSYLMKKMIPLAVEKLLDFDNTLKKNLLNYIDE  
NKLYLIGSAEYEEKSVNKYLKTIMPFDSL IYTNDTILIEMF\*

FIGURE 13

**A: BoNTC<sub>1</sub>(H<sub>N</sub>) synthetic gene SEQ ID NO: 23**

atgTCCCTGTACAACAAGACCCTTGACTGTAGAGAGCTGCTGGTGAAGAA  
CACTGACCTGCCATTCATCGGTGACATCAGTGACGTGAAGACTGACATCT  
TCCTGCGTAAGGACATCAACGAGGAGACTGAGGTGATCTACTACCCAGA  
CAACGTGTGAGTAGACCAAGTGATCCTCAGTAAGAACACCTCCGAGCAT  
GGACAAGTAGACCTGCTCTACCCTAGTATCGACAGTGAGAGTGAGATCC  
TGCCAGGGGAGAATCAAGTCTTCTACGACAACCGTACCCAGAACGTGGA  
CTACCTGAACTCCTACTACTACCTAGAGTCTCAGAAGCTGAGTGACAAC  
GTGGAGGACTTCACTTTCACGCGTTCAATCGAGGAGGCTCTGGACAACA  
GTGCAAAGGTGTACACTTACTTCCCTACCCTGGCTAACAAGGTGAATGCC  
GGTGTGCAAGGTGGTCTGTTCCCTGATGTGGGCAAACGACGTGGTTGAGG  
ACTTCACTACCAACATCCTGCGTAAGGACACACTGGACAAGATCTCAGA  
TGTGTCAGCTATCATCCCCTACATCGGACCCGCACTGAACATCTCCAAC  
CTGTGCGTCGTGGAACTTCACTGAGGCATTTCGAGTCACTGGTGTCACC  
ATCCTGCTGGAGGCATTCCCTGAGTTCACAATCCCTGCTCTGGGTGCATT  
CGTGATCTACAGTAAGGTCCAGGAGCGAAACGAGATCATCAAGACCATC  
GACAAGTGTCTGGAGCAGAGGATCAAGAGATGGAAGGACTCCTACGAGT  
GGATGATGGGAACGTGGTTGTCCAGGATCATCACCCAGTTCAACAACAT  
CTCCTACCAGATGTACGACTCCCTGAACTACCAGGCAGGTGCAATCAAG  
GCTAAGATCGACCTGGAGTACAAGAAGTACTCCGGAAGCGACAAGGAG  
AACATCAAGAGCCAGGTTGAGAACCTGAAGAACAGTCTGGACGTCAAG  
ATCTCGGAGGCAATGAACAACATCAACAAGTTCATCCGAGAGTGCTCCG  
TCACCTACCTGTTCAAGAACATGCTGCCTAAGGTCATCGACGAGCTGAA  
CGAGTTCGACCGAAACACCAAGGCAAAGCTGATCAACCTGATCGACTCC  
CATAACATCATCCTGGTCGGTGAGGTCGACAAGCTGAAGGCAAAGGTAA  
ACAACAGCTTCCAGAACTaa

**B: BoNTC<sub>1</sub>(H<sub>N</sub>) encoded protein SEQ ID NO: 24**

MSLYNKTLDCRELLVKNTDLPFIGDISDVKTDIFLRKDINEETEVIYYPDNVS  
VDQVILSKNTSEHGQLDLLYPSIDSESEILPGENQVFYDNRTQNVLYNSYY  
YLESQKLSDNVEDFTFTRSIEEALDNSAKVYTYFPTLANKVNAGVQGGLFL  
MWANDVVEDFTTNILRKDTLDKISDVSAIIPYIGPALNISNSVRRGNFTEAFA  
VTGVTILLEAFPEFTIPALGAFVIYSKVQERNEIIKTIDNCLEQRIKRWKDSYE  
WMMGTWLSRIITQFNNISYQMYDSLNYQAGAIKAKIDLEYKKYSGSDKENI  
KSQVENLKNSLDVKISEAMNNINKFIRECSVTYLFKNMLPKVIDELNEFDRN  
TKAKLINLIDSHNILLVGEVDKLKAKVNNSFQN\*

FIGURE 14

**A: BoNTD(H<sub>N</sub>) synthetic gene SEQ ID NO: 25**

atggccAACTCCCGTGACGACTCCACCTGCATCAAGGTCAAGAACAACAGA  
CTGCCATACGTTGCCGACAAGGACTCCATCTCCCAGGAGATCTTCGAGA  
ACAAGATCATCACCGACGAGACCAACGTTCAAACTACTCCGACAAGTT  
CTCTTTGGACGAGTCCATCCTGGACGGTCAGGTCCCAATCAACCCAGAG  
ATCGTCGACCCACTGTTGCCAAACGTCAACATGGAGCCATTGAACCTGCC  
AGGTGAGGAGATCGTCTTCTACGACGACATCACCAAGTACGTCGACTAC  
TTGAACTCCTACTACTACTTGGAGTCTCAAAAGTTGTCTAACAACGTCGA  
GAACATCACCTTGACCACCTCCGTCGAGGAGGCCTTGGGTACTCTAACA  
AGATCTACACCTTCCTGCCATCCTTGGCTGAGAAGGTTAACAAGGGTGTT  
CAAGCTGGTTTGTTCCTGAACTGGGCCAACGAGGTCGTCGAGGACTTCA  
CCACCAACATCATGAAGAAGGACACCCTGGACAAGATCTCCGACGTCTC  
CGTCATCATCCCATACATCGGTCCAGCCTTGAACATCGGTAACCTCCGCCC  
TGAGAGGTAACCTCAACCAGGCCTTCGCCACCGCCGGTGTCGCCTTCCTG  
CTGGAGGGTTTCCCAGAGTTCACCATCCCAGCCCTGGGTGTCTTCACCTT  
CTACTCCTCCATCCAGGAGAGAGAGAAGATCATCAAGACCATCGAGAAC  
TGCTTGAGCAGAGAGTCAAGAGATGGAAGGACTCCTACCAGTGGATGG  
TTTCCAACCTGGCTGTCCAGAATCACCAACCAATTCAACCACATCAACTAC  
CAGATGTACGACTCCCTGTCCTACCAGGCCGACGCCATCAAGGCCAAGA  
TCGACCTGGAGTACAAGAAGTACTCCGGTTCGACAAGGAGAACATCAA  
GTCCCAGGTCGAGAACCTGAAGAACTCCTTGGACGTCAAGATCTCCGAG  
GCCATGAACAACATCAACAAGTTCATCCGTGAGTGTTCCGTCACCTACCT  
GTTCAAGAACATGCTGCCAAAGGTCATCGACGAGCTGAACAAGTTCGAC  
CTGAGAACCAAGACCGAGCTGATCAACCTGATCGACTCCCACAACATCA  
TCCTGGTTGGTGAGGTTGACtaa

**B: BoNTD(H<sub>N</sub>) encoded protein SEQ ID NO: 26**

MANSRDDSTCIKVKNNRLPYVADKDSISQEIFENKIITDETNVQNYSDKFSLD  
ESILDGQVPINPEIVDPLLPNVNMEPLNLPGEIIVFYDDITKYVDYLNSYYYL  
ESQKLSNNVENITLTTSVEEALGYSNKIYTFLPSLAEKVNKGVQAGLFLNWA  
NEVEDFTTNIMKKDTLDKISDVSVIPIYGPALNIGNSALRGNFNQAFATAG  
VAFLEGFPEFTIPALGVFTFYSSIQEREKIITIENTCLEQRVKRWKDSYQWM  
VSNWLSRITTQFNHINYQMYDSL SYQADAIKAKIDLEYKKYSGSDKENIKSQ  
VENLKNSLDVKISEAMNNINKFIRECSVTYLFKNMLPKVIDELNKFDLRTKT  
ELINLIDSHNIIIVGEVD\*

FIGURE 15

**A: BoNTE(H<sub>N</sub>) synthetic gene SEQ ID NO: 27**

atgTCCATCTGCATCGAGATCAACAACGGTGAGCTGTTCTTCGTGGCTTCC  
GAGAACAGTTACAACGATGACAACATCAACACTCCTAAGGAGATTGACG  
ACACCGTCACTTCTAACAACAACCTACGAAAACGACCTGGACCAGGTCAT  
CCTAAACTTCAACTCCGAGTCCGCCCTGGTCTGTCCGACGAGAAGCTGA  
ACCTGACCATCCAGAACGACGCTTACATCCCAAAGTACGACTCCAACGG  
TACATCCGATATCGAGCAGCATGACGTTAACGAGCTTAACGTCTTCTTCT  
ACTTAGACGCTCAGAAGGTGCCCGAGGGTGAGAACAACGTCAATCTCAC  
CTCTTCAATTGACACAGCCTTGTTGGAGCAGCCTAAGATCTACACCTTCT  
TCTCCTCCGAGTTCATCAACAACGTCAACAAGCCTGTGCAGGCCGCATTG  
TTCGTAAGCTGGATTTCAGCAGGTGTTAGTAGACTTCACTACTGAGGCTAA  
CCAGAAGTCCACTGTTGACAAGATCGCTGACATCTCCATCGTCGTCCCAT  
ACATCGGTCTGGCTCTGAACATCGGCAACGAGGCACAGAAGGGCAACTT  
CAAGGATGCCCTTGAGTTGTTGGGTGCCGGTATTTTGTGAGTTTCGAAC  
CCGAGCTGCTGATCCCTACCATCCTGGTCTTCACGATCAAGTCCTTCCTG  
GGTTCCTCCGACAACAAGAACAAGGTCATTAAAGGCCATCAACAACGCCC  
TGAAGGAGCGTGACGAGAAGTGGAAGGAAGTCTATTCCTTCATCGTCTC  
GAACTGGATGACCAAGATCAACACCCAGTTCAACAAGCGAAAGGAGCA  
GATGTACCAGGCTCTGCAGAACCAGGTCAACGCCATCAAGACCATCATC  
GAGTCCAAGTACAACCTCCTACACCCTGGAGGAGAAGAACGAGCTTACCA  
ACAAGTACGATATCAAGCAGATCGAGAACGAGCTGAACCAGAAGGTCTC  
CATCGCCATGAACAACATCGACAGGTTCTGACCGAGTCCTCCATCTCCT  
ACCTGATGAAGCTCATCAACGAGGTCAAGATCAACAAGCTGCGAGAGTA  
CGACGAGAATGTCAAGACGTACCTGCTGAACTACATCATCCAGCACGGA  
TCCATCCTGtaa

**B: BoNTE(H<sub>N</sub>) encoded protein SEQ ID NO: 28**

MSICIEINNGELFFVASENSYNDDNINTPKEIDDTVTSNNNYENDLDQVILNF  
NSESAPGLSDEKLNLTIQNDAYIPKYDSNGTSDIEQHVDVNELNVFFYLDAQK  
VPEGENNVNLTSSIDTALLEQPKIYTFSSSEFINNVNKPVQAALFVSWIQQVL  
VDFTTEANQKSTVDKIADISIVVPYIGLALNIGNEAQKGNFKDALELLGAGIL  
LEFEPELLIPTILVFTIKSFLGSSDNKNKVIKAINNALKERDEKWKEVYSFIVS  
NWMTKINTQFNKRKEQMYQALQNQVNAIKTHIESKYNSYTL EEKNELTNKY  
DIKQIENELNQKVSIAMNNIDRFLTESSISYLMKLINEVKINKLREYDENVKT  
YLLNYIIQHGSIL\*

FIGURE 16

**A: BoNTF(H<sub>N</sub>) synthetic gene SEQ ID NO: 29**

atgGCCCCACCACTCTGTGTATTAGAGTCAACAACCTCAGAATTATTCTTT  
GTCGCTTCCGAGTCAAGCTACAACGAGAACGATATTAACACACCTAAAG  
AGATTGACGATACTACCAACCTAAACAACAACCTACCGGAACAACCTGGA  
TGAGGTTATTTTGGATTACAACCTCACAGACCATCCCTCAAATTTCCAACC  
GTACCTTAAACACTCTTGTCCAAGACAACCTCCTACGTTCCAAGATACGAT  
TCTAACGGTACCTCAGAGATCGAGGAGTATGATGTTGTTGACTTTAACGT  
CTTTTTCTATTTGCATGCCCAGAAGGTGCCAGAAGGTGAAACCAACATCT  
CATTGACTTCTTCCATTGATACCGCCTTGTTGGAAGAGTCCAAGGATATC  
TTCTTTTCTTCGGAGTTTATCGATACTATCAACAAGCCTGTCAACGCCGC  
TCTGTTCAATTGATTGGATTAGCAAGGTCATCAGAGATTTTACCACTGAAG  
CTACTCAAAAGTCCACTGTTGATAAGATTGCTGACATCTCTTTGATTGTC  
CCCTATGTCGGTCTTGCTTTGAACATCATTATTGAGGCAGAAAAGGGTAA  
CTTTGAGGAGGCTTTTGAATTGTTGGGAGTTGGTATTTTGTGAGTTTG  
TTCCAGAACTTACCATTCTGTCATTTTAGTTTTTACGATCAAGTCCTACA  
TCGATTTCATACGAGAACAAGAATAAAGCAATTAAGCTATTAACAACCTC  
CTTGATCGAAAGAGAGGCTAAGTGGAAGGAAATCTACTCATGGATTGTA  
TCAAACCTGGCTTACTAGAATTAACACTCAATTTAACAAGAGAAAGGAGC  
AAATGTACCAGGCTCTGCAAAACCAAGTCGATGCTATCAAGACTGCAAT  
TGAATACAAGTACAACAACCTATACTTCCGATGAGAAGAACAGACTTGAA  
TCTGAATACAATATCAACAACATTGAAGAAGAGTTGAACAAGAAAGTTT  
CTTTGGCTATGAAGAATATCGAAAGATTTATGACCGAATCCTCTATCTCT  
TACTTGATGAAGTTGATCAATGAGGCCAAGGTTGGTAAGTTGAAGAAGT  
ACGATAACCACGTTAAGAGCGATCTGCTGAACTACATTCTCGACCACAG  
ATCAATCCTGGGAGAGCAGACAAACGAGCTGAGTGATTTGGTTACTTCC  
ACTTTGAACTCCTCCATTCCATTTGAGCTTTCTtaa

**B: BoNTF(H<sub>N</sub>) encoded protein SEQ ID NO: 30**

MAPPRLCIRVNNSEFFVASESSYNENDINTPKIEDDTTNLNNNYRNNLDEVI  
LDYNSQTIPQISNRTLNTLVQDNSYVPRYDSNGTSEIEEYDVVDFNVFFYLH  
AQKVPEGETNISLTSSIDTALLEESKDIFFSSEFIDTINKPVNAALFIDWISKVIR  
DFTTEATQKSTVDKIADISLIVPYVGLALNIIIEAEKGNFEEAFELLGVGILLEF  
VPELTIPVILVFTIKSYIDSYENKNKAIKAINNSLIEREAKWKEIYSWIVSNWL  
TRINTQFNKRKEQMYQALQNQVDAIKTAIEYKYNNYTSDEKNRLESEYNIN  
NIEEELNKKVSLAMKNIERFMTESISYLMKLINEAKVGKLKKYDNHVKSDL  
LNYILDHRSILGEQTNELSDLVTSTLNSSIPFELS\*



FIGURE 17

**A: BoNTG(H<sub>N</sub>) synthetic gene SEQ ID NO: 31**

atggccAAAAATACCGGTAAATCTGAACAGTGTATTATTGTTAATAATGAG  
GATTTATTTTTCATAGCTAATAAAGATAGTTTTTCAAAGATTTAGCTAA  
AGCAGAACTATAGCATATAATACACAAAATAACTATAGAAAATAAT  
TTTTCTATAGATCAGTTGATTTTAGATAATGATTTAAGCAGTGGCATAGA  
CTTACCAAATGAAAACACAGAACCATTTACAAATTTTGACGACATAGAT  
ATCCCTGTGTATATTAACAATCTGCTTTAAAAAAAATTTTGTGGATGG  
AGATAGCCTTTTTGAATATTTACATGCTCAAACATTTCTTCTAATATAG  
AAAATCTACAATAACGAATTCATTAAATGATGCTTTAAGAAATAATAA  
TAAAGTCTATACTTTTTTTCTACAAACCTTGTTGAAAAAGCTAATACAG  
TTGTAGGTGCTTCACTTTTTGTAACTGGGTAAAAGGAGTAATAGATGAT  
TTTACATCTGAATCCACACAAAAAAGTACTATAGATAAAGTTTCAGATGT  
ATCCATAATTATCCCTATATAGGACCTGCTTTGAATGTAGGAAATGAAA  
CAGCTAAAGAAAATTTTAAAAATGCTTTTGAAATAGGTGGAGCCGCTAT  
CTTAATGGAGTTTATTCCAGAACTTATTGTACCTATAGTTGGATTTTTTAC  
ATTAGAATCATATGTAGGAAATAAAGGGCATATTATTATGACGATATCC  
AATGCTTTAAAGAAAAGGGATCAAAAATGGACAGATATGTATGGTTTGA  
TAGTATCGCAGTGGCTCTCAACGGTTAATACTCAATTTTATACAATAAAA  
GAAAGAATGTACAATGCTTTAAATAATCAATCACAAGCAATAGAAAAAA  
TAATAGAAGATCAATATAATAGATATAGTGAAGAAGATAAAATGAATAT  
TAACATTGATTTTAATGATATAGATTTTAAACTTAATCAAAGTATAAATT  
TAGCAATAACAATATAGATGATTTTATAAACCAATGTTCTATATCATAT  
CTAATGAATAGAATGATTCCATTAGCTGTAAAAAAGTTAAAAGACTTTG  
ATGATAATCTTAAGAGAGATTTATTGGAGTATATAGATACAAATGAACT  
ATATTTACTTGATGAAGTAAATATTCTAAAATCAAAGTAAATAGACAC  
CTAAAAGACAGTATACCATTTGATCTTTCCTACTATATACCtaa

**B: BoNTG(H<sub>N</sub>) encoded protein SEQ ID NO: 32**

MAKNTGKSEQCIIVNNEDLFFIANKDSFSKDLAKAETIAYNTQNNTIENNFSI  
DQLILDNDLSSGIDLPNENTEPFTNFDDIDIPVYIKQSALKKIFVDGDSLFEYL  
HAQTFPSNIENLQLTNSLNDALRNNNKVYTFSTNLVEKANTVVGASLFVN  
WVKGVIDDFTSESTQKSTIDKVSDVSIIPYIGPALNVGNETAKENFKNAFEIG  
GAAILMEFIPELIVPIVGFFTLESYVGNKGHIIMTISNALKKRDQKWTDMYGL  
IVSQWLSTVNTQFYTIKERMYNALNNQSQAIEKIIDQYNRYSEEDKMNINI  
DFNDIDFKLNQSINLAINNIDDFINQCSISYLMNRMIPLAVKKLKDFFDNLKR  
DLLEYIDTNELYLLDEVNILKSKVNRHLKDSIPFDLSLYT\*

FIGURE 18

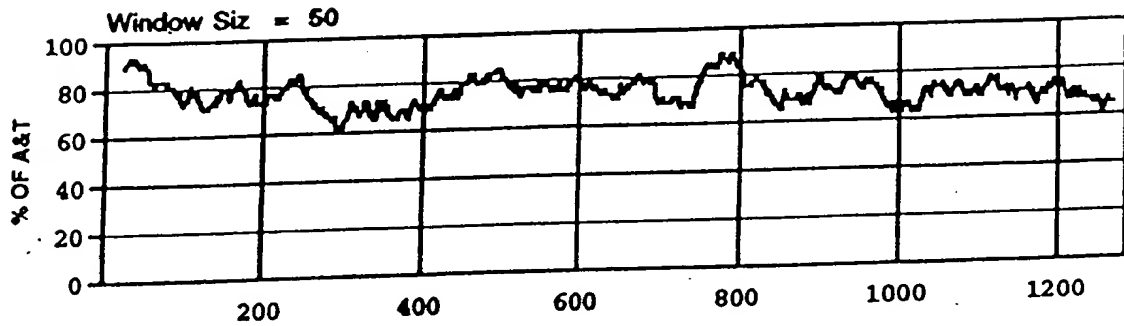
**A: First BoNTF(Hc) gene: SEQ ID NO: 33**

GAATTCACGatgTCTTACACTAACGACAAAATCCTGATCCTGTACTTCAAC  
AAACTGTACAAAAAATCAAAGACAACCTCTATCCTGGACATGCGTTACG  
AAAACAACAAATTCATCGACATCTCTGGCTATGGTTCTAACATCTCTATC  
AACGGTGACGTCTACATCTACTCTACTAACCGCAACCAGTTCGGTATCTA  
CTCTTCTAAACCGTCTGAAGTAAACATCGCTCAGAACAACGACATCATCT  
ACAACGGTCGTTACCAGAACTTCTCTATCTCTTTCTGGGTTTCGTATCCCG  
AAATACTTCAACAAAGTTAACCTGAACAACGAATACACTATCATCGACT  
GCATCCGTAACAACAACCTCTGGTTGGAAAATCTCTCTGAACTACAACAA  
AATCATCTGGACTCTGCAGGACACTGCTGGTAACAACCAGAACTGGTT  
TTCAACTACACTCAGATGATCTCTATCTCTGACTACATTAATAAATGGAT  
CTTCGTTACTATCACTAACAACCGTCTGGGTAACCTCTCGTATCTACATCA  
ACGGTAACCTGATCGATGAAAAATCTATCTCTAACCTGGGTGACATCCA  
CGTTTCTGACAACATCCTGTTCAAATCGTTGGTTGCAACGACACGCGTT  
ACGTTGGTATCCGTTACTTCAAAGTTTTCGACACTGAACTGGGTAAAAC  
GAAATCGAACTCTGTACTCTGACGAACCGGACCCGTCTATCCTGAAAG  
ACTTCTGGGGTAACTACCTGCTGTACAACAAACGTTACTACCTGCTGAAC  
CTGCTCCGGACTGACAAATCTATCACTCAGAACTCTAACTTCCTGAACAT  
CAACCAGCAGCGTGGTGTTTATCAGAAACCTAATATCTTCTCTAACACTC  
GTCTGTACACTGGTGTTGAAGTTATCATCCGTAAAAACGGTTCTACTGAC  
ATCTCTAACACTGACAACTTCGTACGTAAAAACGACCTGGCTTACATCAA  
CGTTGTTGACCGTGACGTTGAATACCGTCTGTACGCTGACATCTCTATCG  
CTAAACCGGAAAAAATCATCAAACCTGATCCGTACTTCTAACTCTAACAA  
CTCTCTGGGTCAGATCATCGTTATGGACTCGATCGGTAAACAACCTGCACTA  
TGAACCTCCAGAACAACAACGGTGGTAACATCGGTCTGCTGGGTTTCCA  
CTCTAACAAACCTGGTTGCTTCTTCATGGTACTACAACAACATCCGTAAAA  
ACACTTCTTCTAACGGTTGCTTCTGGTCTTTCATCTCTAAAGAACACGGTT  
GGCAGGAAAAACtaaGAATTC

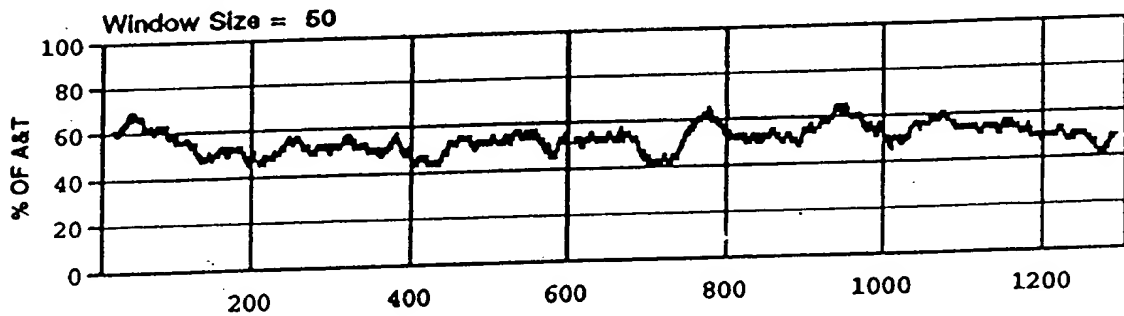
**B: BoNTF(Hc) #1 encoded protein: SEQ ID NO: 34**

MSYTNDKILILYFNKLYKKIKDNSILDMRYENNKFIDISGYGSNISINGDVYIY  
STNRNQFGIYSSKPSEVNIAQNNDIIYNGRYQNFSISFWVRIPKYFNKVNLLN  
EYTIIDCIRNNNSGWKISLNYNKIIWTLQDTAGNNQKLVFNQTQMISISDYIN  
KWIFVTITNNRLGNSRIYINGNLIDEKSISNLGDIHVSDNILFKIVGCNDTRYV  
GIRYFKVFDTEL GKTEIETLYSDEPDPSILKDFWGNLYLLYNKRYYLLNLLRT  
DKSITQNSNFLNINQQRGVYQKPNIFSNTRLYTGVEVIIRKNGSTDISNTDNF  
VRKNDLAYINVVDRDVEYRLYADISIAKPEKIIKLIRTSNSNNSLGQIIVMDSI  
GNNCTMNFQNNNGNIGLLGFHSNNLVASSWYYNNIRKNTSSNGCFWSFIS  
KEHGWQEN\*

### A: Natural BoNTF(Hc) Gene



### B: First BoNTF(Hc) Synthetic Gene



### C: Second BoNTF(Hc) Synthetic Gene

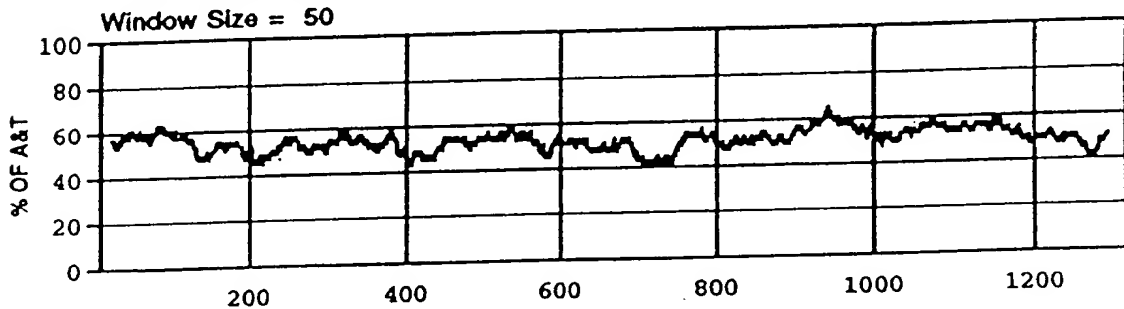
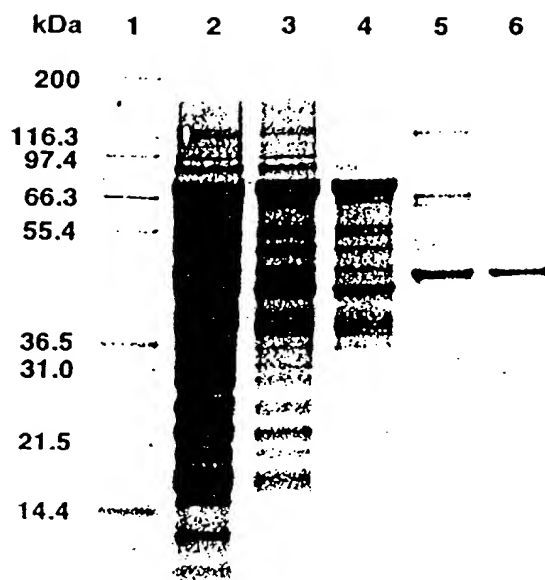


Fig 19

A



B

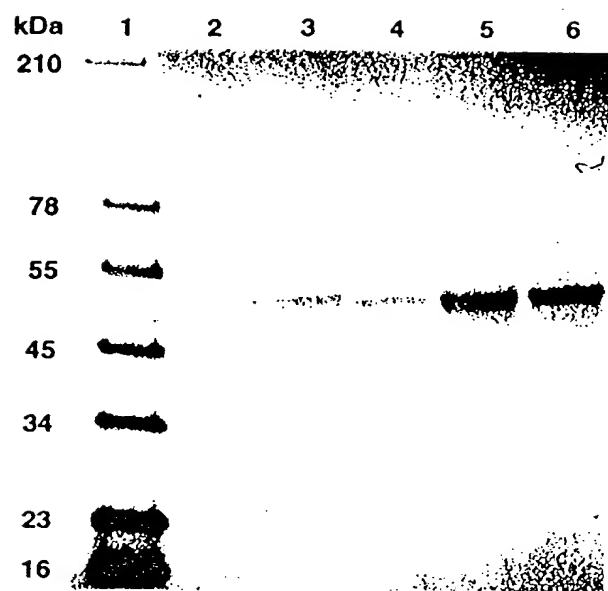


Fig 20

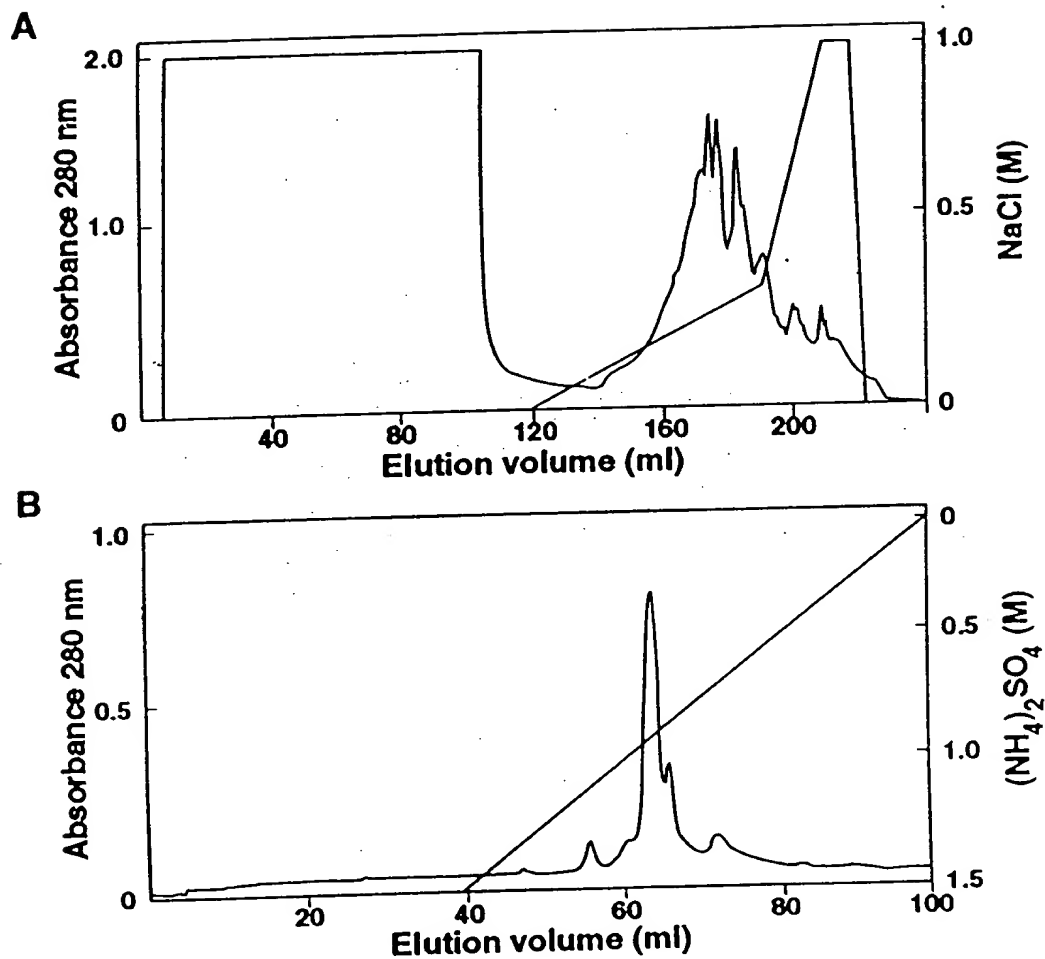


Fig 21

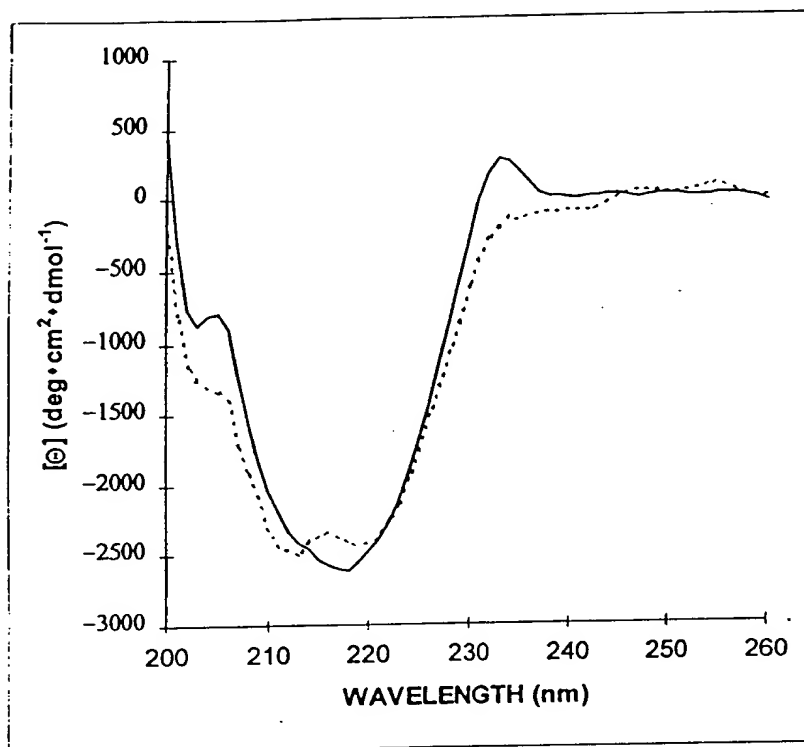


Fig 22